EPI-00312 PATENT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

In re Appl.:	Nyce, J. W.	: Group Art Unit:	1617
Serial No:	To be assigned	: Appl. Ref. No:	EPI-00311
Filed:	Herewith	: Examiner :	S. Jiang

Title: **COMPOSITION, FORMULATIONS & METHOD FOR PREVENTION & TREATMENT OF DISEASES AND CONDITIONS ASSOCIATED WITH BRONCHOCONSTRICTION, ALLERGY(IES) & INFLAMMATION**

PRELIMINARY AMENDMENT

Sir/Madam:

In advance of prosecution, please amend the above-identified application as follows.

IN THE SPECIFICATION

Please amend the specification as follows.

Page 1, line 6, after "This is", insert the following

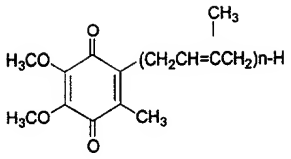
-- a divisional of U.S. Patent Application Serial No. 09/841,426, filed by the present inventor April 24, 2001 and now pending, which is --

IN THE CLAIMS

Please delete claims 1 to 79, without prejudice, and substitute therefor the following claims 80-158.

-- WHAT IS CLAIMED AS NOVEL & UNOBVIOUS IN UNITED STATES LETTERS PATENT:

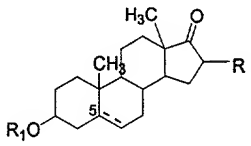
80. A pharmaceutical composition, comprising an agent selected from a ubiquinone and pharmaceutically or veterinarily acceptable salt thereof, wherein the ubiquinone has the chemical formula



(II)

(CoQ_n);

wherein n=1 to 12; and optionally a dehydroepiandrosterone (DHEA) and pharmaceutically or veterinarily acceptable salts thereof, the dehydroepiandrosterone having the chemical formula



(I)

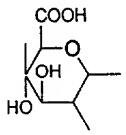
(DHEA) (I)

wherein the broken line represents a single or a double bond; R is hydrogen or a halogen; the H at position 5 is present in the alpha or beta configuration or the compound of chemical formula I comprises a racemic mixture of both configurations; and R^1 is hydrogen or SO_2OM, wherein M is selected from the group consisting of H, Na, sulfatide $-SO_2O-CH_2CHCH_2OCOR^3$; and phosphatide

$$\begin{array}{l} \\ | \\ OCOR^2 \end{array}$$

$$\begin{array}{l} O \\ \| \\ -P-OCH_2CHCH_2OCOR^3 \\ \| \quad\quad | \\ O \quad\quad OCOR^2 \end{array}$$

, wherein R^2 and R^3, which may be the same or different, are straight or branched (C_1-C_{14}) alkyl or glucuronide,



3,4-Dihydroxy-3,5,6-trimethyl-tetrahydro-pyran-2-carboxylic acid

the active agent being present in an amount effective for altering levels of, or sensitivity to, adenosine in a subject's tissue (s), or treating bronchoconstriction, lung inflammation or allergy(ies), chronic obstructive pulmonary disease (COPD) or a disease associated with either of them.

81. The composition of claim 80, wherein in the CoQ_n of formula II, wherein n is 1 to 10.

82. The composition of claim 80, wherein in the CoQ_n of formula II, wherein n is 6 to 10.

83. The composition of claim 82, wherein in the CoQ_n of formula II, wherein n is 10.

84. The composition of claim 83, comprising about 0.1 to about 40% w/w active agent.

85. The composition of claim 84, comprising about 1 to about 20% w/w active agent.

86. The composition of claim 80, wherein the compound of formula (I) is dehydroepiandrosterone, wherein R and R^1 are each hydrogen and the broken line represents a double bond.

87. The composition of claim 80, wherein the compound of formula (I) is 16-alpha bromoepiandrosterone, wherein R is Br, R^1 is H, and the broken line represents a double bond.

88. The composition of claim 80, wherein the compound of formula (I) is 16-alpha-fluoro epiandrosterone, wherein R is F, R^1 is H and the broken line represents a double bond.

89. The composition of claim 80, wherein the compound of formula (I) is etiocholanolone, wherein R and R^1 are each hydrogen and the broken line represents a double bond.

90. The composition of claim 80, wherein the compound of formula (I) is dehydroepiandrosterone sulfate, wherein R is H, R^1 is SO_2OM and M is a sulfatide group as defined above, and the broken line represents a single bond.

91. The composition of claim 80, wherein in the compound of formula (I), R is halogen selected from Br, Cl or F, R^1 is H, and the broken line represents a double bond.

92. The composition of claim 80, wherein the compound of formula (I) is 16-alpha-fluoro epiandrosterone.

93. The composition of claim 80, wherein the compound of formula (I) is selected from dehydroepiandrosterone, 16-alpha-bromoepiandrosterone, 16-alpha-fluoro

epiandrosterone, etiocholanolone, dehydroepiandrosterone sulfate or pharmaceutically or veterinarily acceptable salts thereof.

94. The composition of claim 80, wherein the carrier or diluent comprises a pharmaceutically or veterinarily acceptable carrier or diluent.

95. The composition of claim 94, wherein the carrier or diluent is selected from solid or liquid carriers or diluents, and the active agent comprises liquid or solid particles.

96. The composition of claim 94, further comprising an agent selected from folinic acid, pharmaceutically or veterinarily acceptable salts of folinic acid, other therapeutic agents, preservatives, antioxidants, flavoring agents, volatile oils, buffering agents, dispersants or surfactants.

97. The composition of claim 94, which is a systemic or topical formulation.

98. The formulation of claim 97, in the form of a formulation selected from buccal, sublingual, dermal, intraocular, vaginal, rectal, intraarticular, intrapulmonary respirable, oral, inhalable, nasal, topical, parenteral, or transdermal.

99. The formulation of claim 98, which is an oral formulation selected from the group consisting of capsules, cachets, lozenges, tablets, powder, granules, solutions, suspensions and emulsions.

100. The oral formulation of claim 98, which is a solution, suspension or emulsion selected from the group consisting of aqueous and non-aqueous liquid solutions and suspensions and oil-in-water and water-in-oil emulsions.

101. The oral formulation of claim 98, which is a buccal or sub-lingual formulation selected from the group consisting of lozenges further comprising a flavoring agent selected from the group consisting of sucrose, acacia and tragacanth; and pastilles further comprising an inert base selected from the group consisting of gelatin, glycerin, sucrose and acacia.

102. The oral formulation of claim 99, further comprising an enteric coating.

103. The formulation of claim 80, which is a parenteral formulation.

104. The parenteral formulation of claim 103, in injectable form.

105. The parenteral formulation of claim 103, selected from subcutaneous, intradermal, intramuscular, or intravenous formulations.

106. The injectable formulation of claim 103, selected from injectable solutions or suspensions, and which may further comprise folinic acid, pharmaceutically or veterinarily acceptable salts thereof, other therapeutic agents, antioxidants, buffers, bacteriostatic agents or solutes which render the solution or suspension isotonic with the blood of any intended recipient.

107. The injectable formulation of claim 106, wherein the solutions or suspensions are selected from sterile aqueous or non-aqueous injection solutions or suspensions, which may further comprise suspending agents or thickening agents.

108. The composition of claim 80 in bulk or in single or multi-dose form.

109. The composition of claim 108, wherein the single or multi-dose form is provided in sealed ampoules or vials.

110. The composition of claim 80, which is freeze-dried or lyophilized.

111. The formulation of claim 98, which is a topical formulation selected from ointments, creams, lotions, pastes, gels, sprays, aerosols or oils, which may further comprise a carrier selected from vaseline, lanoline, polyethylene glycols, alcohols or trans-dermal enhancers.

112. The formulation of claim 98, which is a transdermal formulation in the form of a patch.

113. The transdermal formulation of claim 112, which is an iontophoretic formulation selected from iontophoretic solutions or suspensions, and which may further comprise a buffer.

114. The formulation of claim 98, which is an inhalable, respirable, intrapulmonary or nasal formulation.

115. The inhalable or respirable formulation of claim 114, which is an aerosol or spray comprising liquid or solid particles of the active agent, and which may further comprise an ingredient selected from folinic acid, other therapeutic agents, preservatives, antioxidants, flavoring agents, volatile oils, buffering agents, dispersants or surfactants.

116. The formulation of claim 115, comprising an inhalable or respirable formulation comprising powdered or liquid particles of the active agent about 0.05 to about 10 μm in size.

117. The formulation of claim 116, comprising an inhalable or respirable aerosol formulation comprising powdered or liquid particles of the active agent about 0.1 to about 5 μm in size.

118. The formulation of claim 115, which comprises a nasal or intrapulmonary aerosol formulation comprising powdered or liquid particles of the active agent about 10 to about 100 μm in size.

119. The formulation of claim 118, which comprises powdered or liquid particles of the active agent about 10 to about 50 μm in size.

120. The formulation of claim 95, wherein the carrier comprises a hydrophobic carrier.

121. A kit comprising the formulation of claim 94, and a delivery device.

122. The kit of claim 121, wherein the formulation comprises an inhalable, respirable, intrapulmonary or nasal formulation, and the delivery device comprises an inhaler provided with an aerosol generating means.

123. The kit of claim 121, wherein the delivery device delivers individual pre-metered doses of the formulation.

124. The kit of claim 121, wherein the delivery device comprises an inhaler.

125. The kit of claim 121, wherein the inhaler comprises a nebulizer or insufflator.

126. The kit of claim 121, wherein the delivery device comprises a compression inhaler, and the formulation comprises a suspension or solution in an aqueous or non-aqueous liquid or an oil-in-water or water-in-oil emulsion.

127. The kit of claim 120, wherein the formulation is provided in a pierceable or openable capsule or cartridge.

128. An in vivo method of preventing or treating a disorder or condition associated with abnormal levels of adenosine or adenosine receptors, or sensitivity to adenosine in a subject's tissue(s), bronchoconstriction, lung inflammation or allergies, wheezing, difficult breathing, impeded airways, asthma, COPD, CF, ARDS, RDS, decreased lung surfactant,

pulmonary fibrosis, allergic rhinitis, or cancer, comprising administering to a subject in need of treatment a therapeutic amount of the active composition of claim 1.

129. The method of claim 128, wherein the disorder or condition is associated with bronchoconstriction, impeded respiration or wheezing.

130. The method of claim 128, wherein the active agent comprises a dehydroepiandrosterone of chemical formula (I) or its salt.

131. The method of claim 130, wherein the epiandrosterone salt comprises dehydroepiandrosterone sulfate.

132. The method of claim 130, wherein the active agent comprise dehydroepiandrosterone (DHEA).

133. The method of claim 128, wherein epiandrosterone or salt thereof, is administered in an amount of about 0.05 to about 1,000 mg/kg body weight.

134. The method of claim 130, wherein the epiandrosterone or salt thereof is administered in an amount of about 1 to about 600 mg/kg body weight.

135. The method of claim 130, wherein the epiandrosterone or salt thereof is administered in an amount of about 5 to about 200 mg/kg body weight.

136. The method of claim 128, wherein the active agent is a ubiquinone of chemical formula (II) or salt thereof and the method is for treating COPD.

137. The method of claim 136, wherein the ubiquinone or salt thereof is administered in an amount of about 1 to about 1200 mg/kg body weight.

138. The method of claim 137 herein the ubiquinone or salt thereof is administered in an amount of about 30 to about 600 mg/kg body weight.

139. The method of claim 138, wherein the ubiquinone or salt thereof is administered in an amount of about 50 to about 150 mg/kg.

140. The method of claim 128, further comprising administering folinic acid or a salt thereof.

141. The method of claim 140, wherein the folinic acid is administered in an amount about 1 to about 1,000 mg/kg body weight.

142. The method of claim 141, wherein the folinic acid is administered in an amount of about 5 to about 500 mg/kg body weight.

143. The method of claim 128, wherein the disorder or condition is chronic obstructive pulmonary disease (COPD).

144. The method of claim 128, wherein the disorder or condition is acute respiratory distress syndrome (ARDS).

145. The method of claim 128, wherein the disorder or condition comprises lung inflammation or allergy(ies).

146. The method of claim 128, wherein the disorder or condition comprises pulmonary fibrosis.

147. The method of claim 128, wherein the disorder or condition comprises allergic rhinitis.

148. The method of claim 128, wherein the disorder or condition comprises infantile respiratory distress syndrome (RDS).

149. The method of claim 128, wherein the disorder or condition comprises cystic fibrosis (CF).

150. The method of claim 128, wherein the disorder or condition comprises impeded respiration or lung pain.

151. The method of claim 128, wherein the disorder or condition comprises decreased lung surfactant.

152. The method of claim 128, wherein the disorder or condition comprises lung cancer.

153. The method of claim 128, wherein the active agent comprises a ubiquinone and an epiandrosterone or their salts, and they are administered concurrently.

154. The method of claim 153, wherein the epiandrosterone and the ubiquinone or their salts are administered in the same formulation.

155. The method of claim 153, wherein the epiandrosterone and the ubiquinone or their salts are administered in different formulations.

156. The method of claim 128, wherein the subject is a human or non-human animal.

157. The method of claim 128, which is a prophylactic or therapeutic method.

158. The method of claim 128, wherein the subject is in need of treatment to reduce or deplete adenosine levels and/or increase ubiquinone levels. --

REMARKS

THIS APPLICATION

This application is a divisional of U.S. Patent Application Serial No. 09/841,426, filed April 24, 2001, claiming a composition comprising a DHEA compound for the treatment of chronic obstructive pulmonary disease (COPD). In this application, similar claims have been introduced, where the composition comprises a ubiquinone, and optionally a DHEA agent.

THE CLAIMS

Claims 1-79 were filed with the original patent application, and have been deleted. Claims 80-158 have been added and are now pending in this case. Consideration of these claims is requested.

The amendments to the specification and the abstract are of a clerical nature. The amendments to the claims are fully supported by the specification as filed and by the original claims. No objectionable new matter is believed to have been introduced hereby.

Although no further fee is believed to be owed, the Assistant Commissioner is hereby authorized to charge to PTO Account No. **50-1728**, any deficiency in the fees, including an extension fee, which extension, if necessary, is hereby requested. In view of the above amendments and remarks, this application is believed to be in condition for examination and allowance. Early notice to that effect is hereby solicited.

Respectfully submitted.
EpiGenesis Pharmaceuticals, Inc.

October 25, 2001
Date

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R. Haji
SIGNATURE

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